P0608

Safety of Guselkumab in Inflammatory Bowel Disease Up to 1 Year: Integrated Safety Analysis of Phase 2 and 3 Studies in Crohn's Disease and Ulcerative Colitis

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Key Takeaways

- Through 1 year of treatment, guselkumab demonstrated a favorable safety profile in participants with UC or CD
- No anaphylactic or serum sickness reactions were reported through 1 year and rates of malignancy, opportunistic infections, major adverse cardiovascular events, and clinically important hepatic disorders were low
- No new safety concerns were identified when compared to the established safety profile of guselkumab in psoriatic indications

Background

Guselkumab is a dual-acting IL-23p19 subunit inhibitor that neutralizes IL-23 and binds to CD64, a receptor on cells that produce IL-23. It is currently approved in some regions for treatment of ulcerative colitis (UC) and worldwide for the treatment of plaque psoriasis and psoriatic arthritis

While guselkumab has been shown to be safe in UC and Crohn's disease (CD), safety results have only been reported in individual trials to date

Objective

To characterize the overall safety profile of guselkumab in inflammatory bowel disease (IBD), we evaluated pooled safety data from Phase 2/3 clinical trials of guselkumab in UC and CD

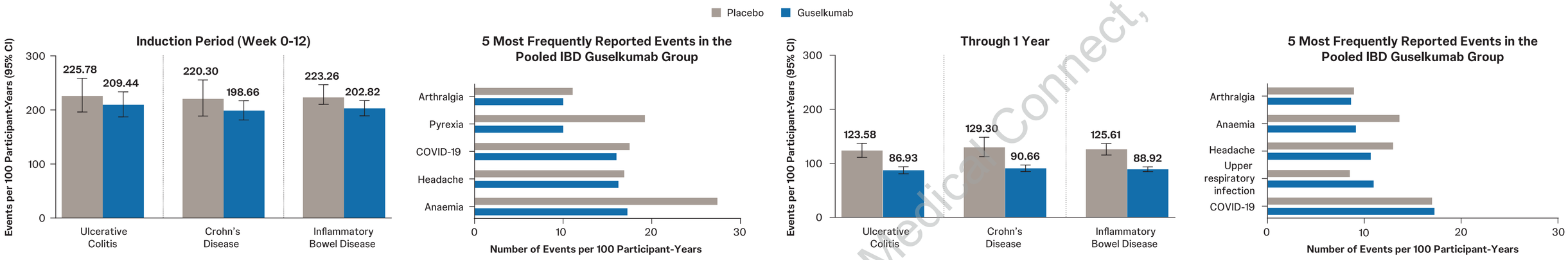
Methods

- Data were pooled from 4 UC studies (n=1514; QUASAR, a Phase 2/3 program and VEGA, a Phase 2a study [guselkumab monotherapy arm only]) and 4 CD studies (n=1492; GALAXI, a Phase 2/3 program and GRAVITI, a Phase 3 study)
- Participants received one of the following treatment regimens, depending on the study:
  - Guselkumab 200 mg IV at Weeks 0, 4, and 8, followed by guselkumab 100 mg SC every 8 weeks or 200 mg SC every 4 weeks (GALAXI, QUASAR)
  - Guselkumab 200 mg IV at Weeks 0, 4, and 8 followed by guselkumab 100 mg SC every 8 weeks (guselkumab monotherapy arm from VEGA)
  - Guselkumab 400 mg SC at Weeks 0, 4, and 8 followed by guselkumab 100 mg SC every 8 weeks or 200 mg SC every 4 weeks (GRAVITI)
  - Placebo (GALAXI, QUASAR, GRAVITI) (Note: participants in the randomized placebo group in the QUASAR Phase 3 maintenance study were clinical responders to guselkumab IV induction before randomization)
- The GALAXI, GRAVITI, and QUASAR studies were pooled for the placebo-controlled induction period through Week 12 (IV and SC; VEGA was excluded from the induction period analysis due to no PBO control)
- The GALAXI, GRAVITI, QUASAR, and VEGA studies were pooled for the through 1-year analysis
- Incidence rates of key safety events were adjusted for the duration of follow-up and reported per 100 participant-years (PY) of follow-up with 95% confidence intervals (CIs)

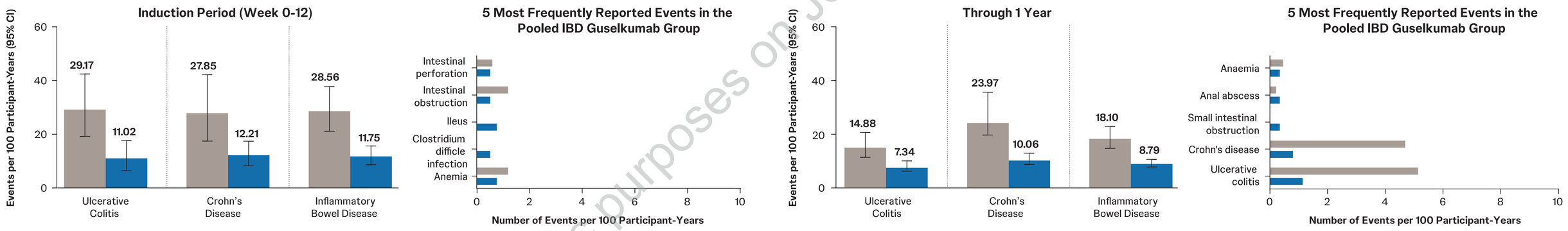
Results

- In the placebo-controlled induction period through Week 12, 1703 participants with IBD were treated with guselkumab with 399.9 participant-years of follow-up and 743 participants were treated with placebo with 171.6 participant-years of follow-up
- Through 1 year, 2057 participants with IBD were treated with guselkumab, with 1752.1 participant-years of follow-up and 886 participants were treated with placebo with 447.4 participant-years of follow-up
- Incidence rates of adverse events, serious adverse events, and adverse events leading to discontinuation were numerically greater in the placebo group than the guselkumab group during the 12-week induction period, as well as through 1 year
- Incidence rates of serious infections were very low throughout both time periods

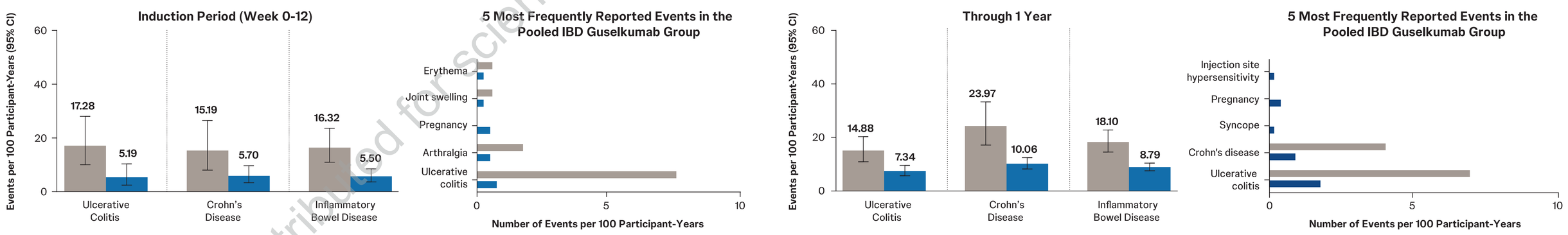
Adverse events



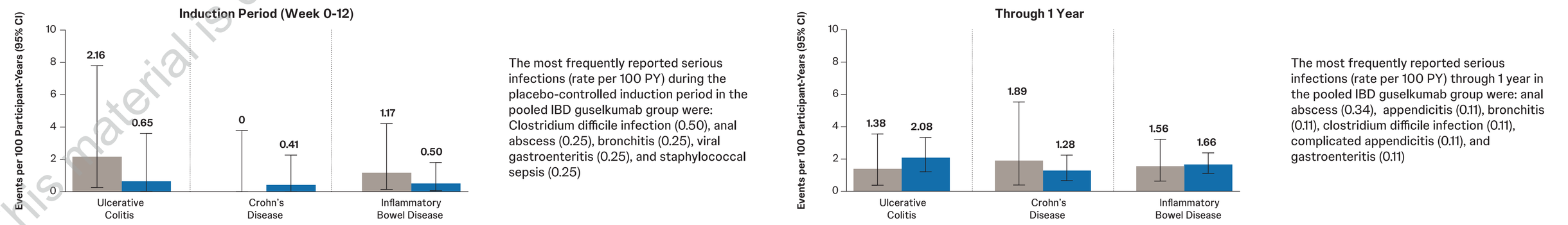
Serious adverse events



Adverse events leading to discontinuation



Serious infections



The most frequently reported serious infections (rate per 100 PY) during the placebo-controlled induction period in the pooled IBD guselkumab group were: Clostridium difficile infection (0.50), anal abscess (0.25), bronchitis (0.25), viral gastroenteritis (0.25), and staphylococcal sepsis (0.25)

The most frequently reported serious infections (rate per 100 PY) through 1 year in the pooled IBD guselkumab group were: anal abscess (0.34), appendicitis (0.11), bronchitis (0.11), clostridium difficile infection (0.11), complicated appendicitis (0.11), and gastroenteritis (0.11)

Targeted adverse events

- Through 1 year, no anaphylactic or serum sickness reactions were reported, and rates of malignancy, opportunistic infections, major adverse cardiovascular events, and clinically important hepatic disorders (hepatic disorder adverse events reported as serious adverse events or adverse events leading to discontinuation of study intervention) were low
- In guselkumab-treated participants, one participant (from an endemic region) reported active tuberculosis
- Two deaths occurred in guselkumab-treated participants (acute myocardial infarction in a participant with pre-existing cardiovascular risk factors and non-suicidal gunshot wound). Two deaths were reported in the placebo group (natural causes and cardiac arrest)

	Induction Period (Week 0-12)[a]		Through 1 Year[b]	
	Placebo (N=743)	IBD Pooled Guselkumab (N=1703)	Placebo[c] (N=886)	IBD Pooled Guselkumab[d] (N=2057)
Total PYs of follow-up	**171.6**	**399.9**	**447.4**	**1752.1**
Events/100 PY (95% CI)[e]				
Deaths	1.17 (0.14, 4.21)	0.50 (0.06, 1.81)	0.45 (0.05, 1.61)	0.11 (0.01, 0.41)
Active tuberculosis	0.00 (0.00, 1.75)	0.00 (0.00, 0.75)	0.00 (0.00, 0.67)	0.06 (0.00, 0.32)
Malignancies	0.00 (0.00, 1.75)	1.25 (0.41, 2.92)	0.89 (0.24, 2.29)	0.74 (0.40, 1.27)
Anaphylactic or serum sickness reactions	0.00 (0.00, 1.75)	0.00 (0.00, 0.75)	0.00 (0.00, 0.67)	0.00 (0.00, 0.17)
Opportunistic Infections	1.75 (0.36, 5.11)	0.50 (0.06, 1.81)	0.67 (0.14, 1.96)	0.23 (0.06, 0.58)
Major adverse cardiovascular events	1.17 (0.14, 4.21)	0.50 (0.06, 1.81)	0.45 (0.05, 1.61)	0.29 (0.09, 0.67)
Clinically important hepatic disorders[f]	0.00 (0.00, 1.75)	0.75 (0.15, 2.19)	0.22 (0.01, 1.25)	0.40 (0.16, 0.82)

[a]Ulcerative colitis: (0-12 weeks) CNTO1959UCO3001 QUASAR Induction Study 1 and Induction Study 2 (VEGA not included due to no placebo control); Crohn's disease (0-12 weeks): CNTO1959CRD3001 GALAXI 1, GALAXI 2, GALAXI 3 and CNTO1959CRD3004 GRAVITI. [b]Ulcerative colitis: CNTO1959UCO3001 (through induction Week 20 for participants who did not enter the Maintenance Study and did not receive treatment at induction Week 12; through induction Week 32 for participants who did not enter the Maintenance Study and received treatment at induction Week 12; through maintenance Week 44 for participants who entered the Maintenance Study); CNTO1959UCO2002 through Week 38 (guselkumab monotherapy arm only); Crohn's disease: CNTO1959CRD3001 GALAXI 1, GALAXI 2 and GALAXI 3, and CNTO1959CRD3004 GRAVITI through Week 48. [c]Ulcerative colitis: includes data up to the first dose of guselkumab for participants who were initially treated with placebo; includes data at or after 12 weeks from the last induction dose of guselkumab for participants who were treated with guselkumab in induction and were rerandomized to placebo in the Maintenance Study, up to the dose adjustment for participants who had a dose adjustment. Crohn's disease: includes data up to the time of rescue or crossover. [d]Ulcerative colitis: CNTO1959UCO3001 QUASAR (through induction Week 20 for participants who did not enter the Maintenance Study and did not receive treatment at induction Week 12; through induction Week 32 for participants who did not enter the Maintenance Study and received treatment at induction Week 12; through maintenance Week 44 for participants who entered the Maintenance Study); CNTO1959UCO2002 VEGA through Week 38 (guselkumab monotherapy arm only); includes all guselkumab data and data up to 12 weeks from the last induction dose of guselkumab for participants who were randomized to placebo in the Maintenance Study. Crohn's disease: CNTO1959CRD3001 GALAXI 1, GALAXI 2 and GALAXI 3, and CNTO1959CRD3004 GRAVITI through Week 48; includes data from the first dose of guselkumab onward for participants who were rescued or crossed over from placebo. [e]Confidence interval based on an exact method assuming that the observed number of events follows a Poisson distribution. [f]Clinically important hepatic disorders are defined as hepatic disorder adverse events reported as serious adverse events or adverse events leading to discontinuation of study intervention. Note: Includes all participants who were treated. Note: Participants are counted only once for any given event, regardless of the number of times they actually experienced the event. Adverse events are coded using MedDRA Version 26.0.

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